



NOTES FILOVIRUSES

MICROBE OVERVIEW

Genetic material

- Single-stranded negative-sense RNA virus family; causes viral hemorrhagic fever

Taxonomy

- Genera: *Ebolavirus*, *Marburgvirus*, *Cuevavirus*

Morphology

- Enveloped virions; filamentous, nonsegmented morphology

Replication

- Transcription, replication mediated by virus-encoded polymerase in infected cell cytoplasm
 - **Transcription:** negative-sense RNA genome transcribed into monocistronic, polyadenylated RNA species using host cell ribosomes, tRNA etc. → translated into seven proteins
 - **Replication:** positive-sense antigenome serves as template for negative-sense genomes

Transmission

- Zoonotic infection
 - **Natural host:** unknown (bats, especially fruit bats considered infection source)
 - **Intermediate host:** Often nonhuman primates (gorillas, chimpanzees)

Structural proteins

- Viral RNA encodes seven structural proteins
 - Nucleoprotein
 - Polymerase cofactor (VP35)
 - Viral proteins VP40, VP24
 - **Glycoprotein:** projecting spikes from lipid bilayer (attachment to host cell receptors)
 - Transcription activator
 - RNA-dependent RNA polymerase

EBOLA VIRUS

osms.it/ebola-virus

PATHOLOGY & CAUSES

- **Ebola virus:** causative agent of severe, often fatal hemorrhagic fever
- **Species:** Zaire, Sudan, Tai Forest, Bundibugyo, Reston
- **Transmission**
 - **Animal-human:** direct infected-animal tissue, body-fluid contact; butchering, consuming undercooked meat

- **Human-human:** direct tissue, body fluid contact with ill/deceased
- **Potential transmission:** contaminated surface/object contact

PATHOLOGY

- **Inoculation → incubation:** 6–12 days average (ranges 2–21 days)
 - Host cell attachment, virus endocytosis → nucleocapsid release in cytoplasm →

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- replication → nucleocapsid formation → viral shedding, cell necrosis
- Initially **macrophages**, **dendritic cells** infected → sentinel lymph node spread → bloodstream → many cell types infected (**endothelial cells**, fibroblasts, **hepatocytes**, epithelial cells, adrenal-gland cells) with lymphocyte/neuron exception
 - Although uninfected, inflammatory mediators; support signal loss from dendritic cells → “bystander” apoptosis of lymphocytes
- Multifocal necrosis in various tissues (e.g. liver, spleen)
- **Systemic inflammatory syndrome**: proinflammatory mediator, cytokine release from infected macrophages, dendritic cells, necrotic cell breakdown products, etc. → vasodilation, ↑ vascular permeability → vascular leakage, shock, multiorgan failure
- Dendritic cell dysfunction, “bystander” lymphocyte apoptosis → impaired adaptive immunity

RISK FACTORS

- Healthcare workers without appropriate protective equipment, adequate training
- Inadequate infected waste product, corpse handling
- Sexual intercourse with person recovering from Ebola in previous three months
- Travel to endemic/Ebola epidemic areas
- Wild animal contact (mostly nonhuman primates)

COMPLICATIONS

- Gastrointestinal dysfunction
 - Fluid loss, hypotension, acute kidney injury, **shock**
- Neurologic
 - Meningoencephalitis, meningitis
- Coagulopathy
 - Infected macrophages produce tissue factor (TF), stimulate extrinsic coagulation pathway → **disseminated intravascular coagulation (DIC)**
- Respiratory failure
- Coinfection/superinfection
- Impaired adaptive immunity → bacterial sepsis

- Spontaneous abortion, vaginal bleeding in infected pregnant individuals (100% third trimester maternal, fetal mortality)
- Fatality ranges
 - 40% to 80–90% (depending upon species)



Figure 72.1 A scanning electron micrograph of an ebola virus demonstrating the typical filamentous structure seen in its class, *Filoviridae*.

SIGNS & SYMPTOMS

Initial nonspecific symptoms

- Fever, chills, fatigue, headache, appetite loss, malaise, sore throat, **myalgias**, lumbosacral pain

Dermatological

- Diffuse erythematous; nonpruritic maculopapular/morbilliform rash, especially on torso/face

Gastrointestinal

- Watery **diarrhea** (up to 10L/2.2gal); nausea; **vomiting**; epigastric, abdominal pain; abdominal tenderness

Hemorrhage

- Commonly hematochezia, followed by hematemesis, melena, metrorrhagia, purpura, petechiae, ecchymoses, mucosal bleeding, venipuncture site bleeding
 - Often occur later in disease course; not all infected individuals develop significant bleeding; host susceptibility-dependent (genetically determined viral immune response difference), different species' pathogenicity

Neurologic

- Meningoencephalitis symptoms (altered level of consciousness, hyperreflexia, myopathy, stiff neck, gait instability, seizure)

Ocular

- Conjunctival injection, uveitis symptoms (blurred vision, photophobia, blindness)

Respiratory

- Tachypnea, dyspnea

Convalescent period

- Can persist > two years often followed by symptoms such as arthralgia, blurred vision, retro-orbital pain, hearing loss, alopecia, difficulty swallowing, insomnia
- Infectious virus/viral RNA can persist in body fluid (semen, breast milk, urine, cerebrospinal fluid, aqueous humor) < nine months after not detectable in blood → variable transmission risk

DIAGNOSIS

- Diagnostic criteria
 - Clinical manifestation
 - Travel to endemic/Ebola epidemic areas (within three weeks prior to disease onset)
 - Infected individual contact during acute disease

LAB RESULTS

- Reverse-transcription polymerase chain reaction (RT-PCR)
 - Detectable Ebola virus in blood samples within three days after symptom onset
- Rapid chromatographic immunoassay (ReBOV)

- Laboratory findings
 - Leukopenia; thrombocytopenia; ↑ ↓ hematocrit; ↑ aspartate aminotransferase (AST), alanine aminotransferase (ALT)
 - Prolonged prothrombin (PT), partial thromboplastin time (PTT)
 - Proteinuria, ↑ blood urea nitrogen, ↑ creatinine
 - Hyponatremia, hypocalcemia, hyperkalemia

TREATMENT

- No cure
- Infected individual **isolation**; placement in negative airflow room advised

MEDICATIONS

- Complications treatment
 - **Coinfection/superinfection**: empiric antimicrobial therapy with broad spectrum antibiotics
 - **Shock**: intravenous fluids, vasoconstrictors
 - **Fever reduction**: antipyretic agents

OTHER INTERVENTIONS

- Complications treatment
 - Fluid, electrolyte loss correction
 - **Acute kidney injury**: renal replacement therapy (dialysis)
 - **Respiratory failure**: supplemental oxygen therapy, mechanical ventilation (if necessary, barotrauma risk)